

Claims

1. A method of preparing a targeting composition having tumour-targeting capacity, comprising covalently attaching the cyclic GRENYHGCTTHWGFTLC peptide (CTT2 peptide)
5 or a derivative thereof to a synthetic derivative of polyethylene glycol.
2. The method according to claim 1, wherein the synthetic derivative of polyethylene glycol is DSPE-PEG.
- 10 3. The method according to claim 2, wherein the DSPE-PEG is DSPE-PEG-NHS.
4. The method according to claim 1, wherein the derivative of the CTT2 peptide is a peptide selected from the group consisting of KRENYHG-cyclo-(CTTHWGFTLC), K(DOTA)RENYHG-cyclo-(CTTHWGFTLC), K(DOTA(In))RENYHG-cyclo-(CTTHW-
15 GFTLC); Ac-GRENYHG-cyclo-(CTTHWGFTLC)K-NH₂, Ac-GRENYHG-cyclo-(CTTHWGFTLC)K(DOTA)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-6-Fluoro-W)GFTLC)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-5-Fluoro-W)GFTLC)-NH₂ and GRENYHG-Cyclo(CTTH(*d,l*-5-OH-W)GFTLC)-NH₂.
- 20 5. The method according to claim 4, wherein the synthetic derivative of polyethylene glycol is DSPE-PEG-NHS.
6. A method for preparing a therapeutic or imaging liposome composition, comprising the steps of
25 (a) obtaining liposomes carrying at least one chemotherapeutic agent or an imaging agent,
(b) preparing a targeting composition having tumour-targeting capacity, by covalently attaching the cyclic GRENYHGCTTHWGFTLC peptide (CTT2 peptide) or a derivative thereof to a synthetic derivative of polyethylene glycol, and
30 (c) combining the liposomes and the targeting composition to form a suspension.
7. The method according to claim 6, wherein the derivative of the CTT2 peptide is a peptide selected from the group consisting of KRENYHG-cyclo-(CTTHWGFTLC), K(DOTA)RENYHG-cyclo-(CTTHWGFTLC), K(DOTA(In))RENYHG-cyclo-(CTTHW-

GFTLC), Ac-GRENYHG-cyclo-(CTTHWGFTLC)K-NH₂, Ac-GRENYHG-cyclo-(CTTHWGFTLC)K(DOTA)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-6-Fluoro-W)GFTLC)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-5-Fluoro-W)GFTLC)-NH₂ and GRENYHG-Cyclo(CTTH(*d,l*-5-OH-W)GFTLC)-NH₂.

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8. A method for treating cancer in a patient, comprising the steps of

(a) obtaining liposomes carrying at least one chemotherapeutic agent,

(b) obtaining a targeting composition comprising

(1) the cyclic GRENYHGCTTHWGFTLC peptide (CTT2 peptide) or a deriva-

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tive thereof and

(2) a synthetic derivative of polyethylene glycol,

(c) combining the liposomes and the targeting composition to form a suspension, and

(d) administering the suspension obtained to the patient.

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9. The method according to claim 8, wherein the derivative of CTT2 peptide is a peptide selected from the group consisting of KRENYHG-cyclo-(CTTHWGFTLC), K(DOTA)RENYHG-cyclo-(CTTHWGFTLC), K(DOTA(In))RENYHG-cyclo-(CTTHWGFTLC), Ac-GRENYHG-cyclo-(CTTHWGFTLC)K-NH₂, Ac-GRENYHG-cyclo-(CTTHWGFTLC)K(DOTA)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-6-Fluoro-W)GFTLC)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-5-Fluoro-W)GFTLC)-NH₂ and GRENYHG-Cyclo(CTTH(*d,l*-5-OH-W)GFTLC)-NH₂.

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10. The method according to any one of claims 6 to 9, wherein the chemotherapeutic agent is doxorubicin.

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11. A diagnostic or imaging test kit for carrying out a diagnostic method for detecting a suspected tumour in a patient, wherein the test kit comprises

- a targeting composition comprising the cyclic GRENYHGCTTHWGFTLC peptide (CTT2 peptide) or a derivative thereof and a synthetic derivative of polyethylene glycol,

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and

- liposomes carrying at least one imaging agent.

12. The test kit according to claim 11, wherein the derivative of CTT2 peptide is a peptide selected from the group consisting of KRENYHG-cyclo-(CTTHWGFTLC),

K(DOTA)RENYHG-cyclo-(CTTHWGFTLC), K(DOTA(In))RENYHG-cyclo-(CTTHWGFTLC), Ac-GRENYHG-cyclo-(CTTHWGFTLC)K-NH₂, Ac-GRENYHG-cyclo-(CTTHWGFTLC)K(DOTA)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-6-Fluoro-W)GFTLC)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-5-Fluoro-W)GFTLC)-NH₂ and GRENYHG-Cyclo-(CTTH(*d,l*-5-OH-W)GFTLC)-NH₂.

13. A diagnostic or imaging composition, comprising
 - a targeting composition comprising the cyclic GRENYHGCTTHWGFTLC peptide (CTT2 peptide) or a derivative thereof and a synthetic derivative of polyethylene glycol,
 10 and
 - liposomes carrying at least one imaging agent.

14. The composition according to claim 13, wherein the derivative of CTT2 peptide is a peptide selected from the group consisting of KRENYHG-cyclo-(CTTHWGFTLC),
 15 K(DOTA)RENYHG-cyclo-(CTTHWGFTLC), K(DOTA(In))RENYHG-cyclo-(CTTHWGFTLC), Ac-GRENYHG-cyclo-(CTTHWGFTLC)K-NH₂, Ac-GRENYHG-cyclo-(CTTHWGFTLC)K(DOTA)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-6-Fluoro-W)GFTLC)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-5-Fluoro-W)GFTLC)-NH₂ and GRENYHG-Cyclo-(CTTH(*d,l*-5-OH-W)GFTLC)-NH₂.

20 15. Use of a preparation comprising as a suspension
 (1) a targeting composition, which comprises
 (a) the cyclic GRENYHGCTTHWGFTLC peptide (CTT2 peptide) or a derivative thereof and covalently attached thereto
 25 (b) a synthetic derivative of polyethylene glycol, and
 (2) liposomes carrying at least one chemotherapeutic agent,
 for the manufacture of a pharmaceutical composition useful for the treatment of cancer.

16. Use according to claim 15, wherein the derivative of CTT2 peptide is a peptide selected from the group consisting of KRENYHG-cyclo-(CTTHWGFTLC), K(DOTA)RENYHG-cyclo-(CTTHWGFTLC), K(DOTA(In))RENYHG-cyclo-(CTTHWGFTLC),
 30 Ac-GRENYHG-cyclo-(CTTHWGFTLC)K-NH₂, Ac-GRENYHG-cyclo-(CTTHWGFTLC)K(DOTA)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-6-Fluoro-W)GFTLC)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-5-Fluoro-W)GFTLC)-NH₂ and GRENYHG-Cyclo-(CTTH(*d,l*-5-OH-W)GFTLC)-NH₂.

YHG-Cyclo(CTTH(*d,l*-5-Fluoro-W)GFTLC)-NH₂ and GRENYHG-Cyclo-(CTTH(*d,l*-5-OH-W)GFTLC)-NH₂.

17. A peptide selected from the group consisting of KRENYHG-cyclo-(CTTHWGFTLC),
5 K(DOTA)RENYHG-cyclo-(CTTHWGFTLC), K(DOTA(In))RENYHG-cyclo-(CTTHW-
GFTLC), Ac-GRENYHG-cyclo-(CTTHWGFTLC)K-NH₂, Ac-GRENYHG-cyclo-
(CTTHWGFTLC)K(DOTA)-NH₂, GRENYHG-Cyclo(CTTH(*d,l*-6-Fluoro-W)GFTLC)-
NH₂, GRENYHG-Cyclo(CTTH(*d,l*-5-Fluoro-W)GFTLC)-NH₂ and GRENYHG-Cyclo-
(CTTH(*d,l*-5-OH-W)GFTLC)-NH₂.

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18. A process for purifying the targeting composition obtainable by covalently attaching
the cyclic GRENYHGCTTHWGFTLC peptide (CTT2 peptide) or a derivative thereof to a
synthetic derivative of polyethylene glycol, the process comprising the steps of
(a) treating the reaction mixture with an organic solvent to obtain a precipitate,
15 (b) centrifuging, washing with an organic solvent and recentrifuging the precipitate to ob-
tain a pellet,
(c) suspending the pellet in a buffer and
(d) carrying out size-exclusion chromatography to obtain pure targeting composition.
- 20 19. The process according to claim 18, wherein the organic solvent in steps (a) and (b) is
diethyl ether and the buffer in step (c) is ammonium acetate - TFA buffer, pH 4.5.